

I. AMENDMENT

In the Claims:

The following listing of claims will replace all prior versions and listings of the claims in the application:

Listing of the Claims:

- 1 – 4. (Cancelled)
5. (Previously presented) A recombinant adenovirus that comprises SEQ ID NO:1 or SEQ ID NO:2.
- 6-10. (Canceled)
11. (Previously presented) The method of claim 13 wherein the adenovirus death protein comprises SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, or SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11 or SEQ ID NO:12.
12. (Previously presented) The method of claim 13, wherein the adenovirus vector comprises a recombinant adenovirus lacking expression of at least one E3 protein selected from the group consisting of: gp19K; RID α ; RID β and 14.7K.
13. (Previously presented) A method for treating cancer in an animal having a tumor comprising administering to the tumor an adenovirus vector wherein
- said adenovirus vector is replication-competent in neoplastic cells and overexpresses an adenovirus death protein (ADP), wherein overexpression is defined as overexpression relative to *d1309*.

14. (Previously presented) The method of claim 13, further comprising the step of passively immunizing the animal against the adenovirus vector.

15. (Previously presented) The method of claim 14, wherein the adenovirus vector comprises SEQ ID NO:1 or SEQ ID NO:2.

16. (Original) The method of claim 12, wherein the vector is replication-restricted to neoplastic cells.

17. (Original) The method of claim 16, wherein the vector is a recombinant adenovirus comprising SEQ ID NO:1 or SEQ ID NO:2.

18. (Currently amended) The method of claim 12, wherein the ~~recombinant adenovirus vector~~ comprises a ~~tissue~~tumor specific promoter ~~or an inducible promoter substituted for the E4 promoter.~~

19. (Currently amended) The method of claim 18, wherein the recombinant adenovirus ~~which~~ comprises SEQ ID NO:14, SEQ ID NO:15 or SEQ ID NO:16.

20. (Original) The method of claim 13, further comprising treating the tumor with radiation.

21. (Previously presented) The method of claim 20 comprising administering more than one distinct type of recombinant adenovirus to the tumor and treating the tumor with radiation, wherein at least one recombinant adenovirus is replication-defective.

22. (Original) The method of claim 13, further comprising treating the tumor with chemotherapy.

23. (Original) The method of claim 22 comprising administering more than one recombinant adenovirus to the tumor and treating the tumor with chemotherapy.

24. (Previously presented) The method of claim 13, further comprising administering to the tumor one or more replication-defective adenoviruses, wherein each replication-defective adenovirus expresses an anti-cancer gene product, and wherein the adenovirus vector facilitates the spread of the replication-defective adenovirus in the tumor.

25-27. (Canceled)

28. (Currently amended) The method of claim 13, wherein the adenovirus vector is ~~replication defective, or it is replication-restricted~~ to dividing cells or neoplastic cells.

29. (Currently amended) The method of claim ~~[[28]]~~13, wherein the adenovirus vector comprises a mutation in an E1A gene that renders the adenovirus incapable of expressing an E1A viral protein which binds the pRB and the p300/CBP proteins.

30. (Original) The method of claim 28, wherein an E4 promoter of said recombinant adenovirus vector is substituted with a promoter, which is activated in neoplastic cells.

31. (Original) The method of claim 30, wherein the promoter, which is activated in neoplastic cells, is the surfactant protein B ("SPB") promoter.

32. (Previously presented) The method of claim 13, wherein overexpression relative to *dl309* is detectable by western blot, cell lysis, virus release or by a cell spreading assay.

33. (Previously presented) The method of claim 13, wherein the adenovirus vector lacks expression of at least one E3 protein selected from the group consisting of gp19K, RID α , RID β and 14.7K.

34. (Previously presented) The method of claim 33, wherein the adenovirus vector lacks expression of the gp19K protein.

35. (Previously presented) The method of claim 33, wherein the adenovirus vector lacks expression of the RID α protein.

36. (Previously presented) The method of claim claim 33, wherein the adenovirus vector lacks expression of the RID β protein.

37. (Previously presented) The method of claim 33, wherein the adenovirus vector lacks expression of the 14.7K protein.

38. (Previously presented) The method of claim 33, wherein the adenovirus vector lacks expression of the gp19K, RID α , RID β and 14.7K proteins.

39. (Previously presented) The method of claim 28, wherein the adenovirus vector comprises a deletion in the E3 region that removes a splice site for any of the E3 mRNAs.

40. (Previously presented) The method of claim 13, wherein the adenovirus vector comprises at least one deletion in the E3 region, wherein the at least one deletion comprises a sequence that encodes at least one E3 protein, wherein the protein is selected from the group consisting of gp19K, RID α , RID β , and 14.7K.

41. (Previously presented) The method of claim 40, wherein the at least one deletion comprises a sequence that encodes the gp19K, RID α , RID β and 14.7K proteins.

42. (Previously presented) The method of claim 41, wherein the at least one deletion further comprises a sequence that encodes the 6.7K protein.

43. (Previously presented) The method of claim 41, wherein the at least one deletion further comprises a sequence that encodes the 12.5K protein.

44. (Previously presented) The method of claim 41, wherein the at least one deletion further comprises a sequence that encodes the 6.7K and 12.5K proteins.

45 – 59. (Canceled)

60. (Previously presented) A method for treating cancer in an animal having a tumor, the method comprising administering to the tumor an adenovirus vector that is replication-competent in neoplastic cells and expresses an adenovirus death protein (ADP), wherein:

- a) the ADP is expressed from an ADP coding sequence positioned under the control of a promoter other than the endogenous promoters for ADP;
- b) the adenovirus vector comprises a deletion in the E3 region that removes a splice site for an E3 mRNA;
- c) the ADP is expressed from an ADP coding sequence flanked by a pre-mRNA splicing and cleavage/polyadenylation signal other than the pre-mRNA splicing and cleavage/polyadenylation signal normally associated with the ADP gene, and/or
- d) the ADP is expressed from an ADP coding sequence that is positioned downstream of the coding sequence for another adenovirus mRNA, together with a sequence on the 5' side of the ADP coding sequence that allows for internal initiation of translation of ADP.

61. (Previously presented) The method of claim 60 wherein the ADP comprises the sequence of SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11 or SEQ ID NO:12.

62. (Previously presented) The method of claim 60, further comprising the step of passively immunizing the animal against the adenovirus vector.

63. (Canceled)

64. (Previously presented) The method of claim 60, further comprising treating the tumor with radiation.

65. (Previously presented) The method of claim 64 comprising administering more than one distinct type of recombinant adenovirus to the tumor and treating the tumor with radiation, wherein at least one recombinant adenovirus is replication-defective.

66. (Previously presented) The method of claim 60, further comprising treating the tumor with chemotherapy.

67. (Previously presented) The method of claim 60, further comprising administering to the tumor one or more replication-defective adenoviruses, wherein each replication-defective adenovirus expresses an anti-cancer gene product, and wherein the adenovirus vector facilitates the spread of adenoviruses in the tumor.

68. (Previously presented) The method of claim 60, wherein the ADP is expressed from an ADP coding sequence positioned under the control of promoter other than the endogenous promoters for ADP.

69. (Previously presented) The method of claim 68, wherein the ADP coding sequence is positioned under the control of a promoter that is exogenous to adenovirus.

70. (Previously presented) The method of claim 60, wherein the ADP coding sequence is positioned behind a coding sequence for another adenovirus mRNA together with a sequence on the 5' side of the ADP coding sequence that allows for internal initiation of translation of ADP.

71. (Previously presented) The method of claim 70, wherein the sequence on the 5' side of the ADP coding sequence that allows for internal initiation of translation of ADP is an Ad tripartite leader or a viral internal ribosome initiation sequence.

72. (Previously presented) The method of claim 60, wherein the adenovirus vector comprises a deletion in the E3 region that removes a splice site for an E3 mRNA.

73. (Previously presented) The method of claim 72, wherein the adenovirus vector lacks expression of at least one E3 protein selected from the group consisting of gp19K, RID α , RID β , and 14.7K.

74. (Previously presented) The method of claim 73, wherein the adenovirus vector lacks expression of each of gp19K, RID α , RID β , and 14.7K.

75. (Previously presented) The method of claim 74, wherein the adenovirus additionally lacks expression of the E3 6.7K and 12.5K proteins.

76. (Canceled)

77. (Currently amended) The method of claim ~~[[76]]~~60, wherein the adenovirus vector is replication-restricted to neoplastic cells.

78. (Original) The method of claim 60, wherein the adenovirus vector comprises a mutation in its E1 region.

79. (Original) The method of claim 78, wherein the adenovirus vector comprises a 1101/1107 mutation in its E1A coding region.

80. (Currently amended) The method of claim 60, wherein the adenovirus vector comprises an adenoviral gene essential for replication positioned under the control of a ~~tissue specific or~~ tumor specific promoter.

81-96. (Canceled)

97. (Previously presented) The method of claim 60, wherein the adenovirus vector is an Ad1, Ad2, Ad5 or Ad6 vector.

98. (Previously presented) The method of claim 60, wherein the adenovirus vector is administered to the tumor by injection of vector intravenously or intrathecally.

99. (Previously presented) The method of claim 60, wherein the adenovirus vector is administered to the tumor by direct injection of the tumor.

100. (Previously presented) The method of claim 60, wherein the animal is passively immunized against the recombinant adenovirus.

101-102. (Canceled)

103. (Previously presented) The method of claim 32, wherein the overexpression relative to a control virus is detectable by western blot

104. (Previously presented) The method of claim 32, wherein the overexpression relative to a control virus is detectable by cell lysis

105. (Previously presented) The method of claim 32, wherein the overexpression relative to a control virus is detectable by virus release

106. (Previously presented) The method of claim 32, wherein the overexpression relative to a control virus is detectable by a cell spreading assay.

107. (Previously presented) The method of claim 60, wherein the animal is a human.
108. (Previously presented) The method of claim 13, wherein the animal is a human.